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Case Letter

Atypical presentation of a solitary neurofibroma with histopathological heterogeneity

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Sir,

Solitary neurofibroma is a common benign peripheral nerve sheath tumor that typically presents as a small, soft, skin-colored papule or nodule. Although the diagnosis is generally straightforward, atypical clinical morphology may obscure recognition and raise concern for malignancy, necessitating careful clinicopathological correlation [1,2]. Compared with conventional neurofibromas, cases showing both unusual gross morphology and diverse cellular components remain insufficiently characterized, and their diagnostic pitfalls are not fully appreciated.

A 73-year-old man presented with a long-standing cutaneous lesion on his right thigh. The lesion had first been noticed approximately 10 years prior as a small brownish-red eruption and had gradually increased in size over time. His medical history was significant for hypertension and prostate cancer, for which he had undergone surgical treatment without recurrence or metastasis. There was no family history suggestive of neurofibromatosis. On physical examination, a pedunculated, brownish-red tumor measuring 6 x 3 cm was observed on the right thigh (Fig. 1a). The lesion was soft to elastic in consistency and non-tender. Given its progressive enlargement and atypical morphology, a malignant neoplasm, including soft tissue sarcoma, could not be ruled out. Therefore, complete surgical excision was performed for both diagnostic and therapeutic purposes.

Histopathological examination revealed a poorly circumscribed tumor extending from the dermis into the subcutaneous adipose tissue (Fig. 1b). The lesion consisted of a heterogeneous population of small to medium-sized round to short spindle-shaped cells embedded within a myxoid stroma (Fig. 1c). Scattered mast cells were also noted throughout the lesion. No mitotic figures or significant cytological atypia were identified. In addition, focal areas demonstrated structures suggestive of Schwann cell differentiation, including elongated nuclei with wavy contours (Fig. 1d). While classical neurofibromas are composed of relatively uniform spindle cells, the present case demonstrated conspicuous cellular heterogeneity, including round to short spindle cells within a mucin-rich matrix, which may mimic other neoplasms.

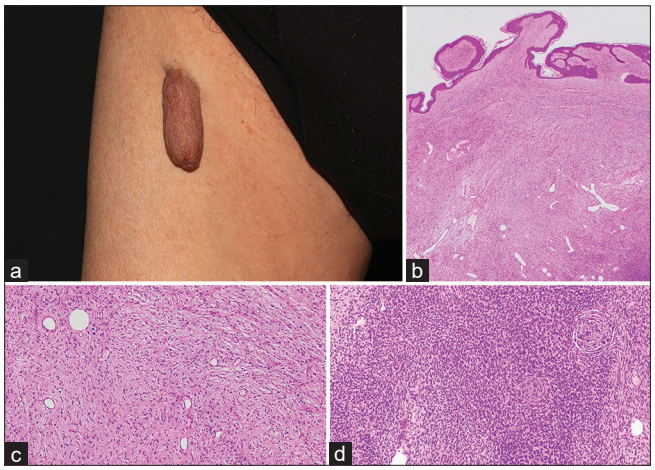

Figure 1: Clinical and histopathological findings. (a) A pedunculated brownish-red tumor measuring 6 x 3 cm on the right thigh. (b) Low-power view showing a poorly circumscribed tumor extending from the dermis into the subcutaneous adipose tissue (H&E stain). (c) High-power view demonstrating proliferation of small to medium-sized round to short spindle-shaped cells within a myxoid stroma, with scattered mast cells (H&E stain). (d) High-power view revealing Schwann cell-like features with elongated, wavy nuclei, supporting neural differentiation (H&E stain).

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Given the histological diversity, the differential diagnosis included neurofibroma, schwannoma, and atypical neurofibroma. Immunohistochemical analysis was therefore undertaken. The tumor cells were diffusely positive for S-100 protein, supporting neural origin. Calretinin staining was negative, arguing against schwannoma, which often exhibits calretinin positivity [3]. Furthermore, p16 expression was preserved, making atypical neurofibroma less likely, as loss of p16 expression has been associated with atypical or premalignant peripheral nerve sheath tumors. Based on the combination of clinical, histopathological, and immunohistochemical findings, a diagnosis of solitary neurofibroma with histopathological heterogeneity was established. The patient's postoperative course was uneventful, and no recurrence has been observed to date.

Solitary neurofibromas typically exhibit uniform histological features characterized by spindle cells with wavy nuclei in a collagenous matrix. Previous reports have demonstrated that solitary neurofibromas may present with atypical clinical features, mimicking other conditions such as vascular malformations or occurring at unusual anatomical sites [4,5]. However, variations such as myxoid change, increased cellularity, or the presence of round cells may occur and can mimic other peripheral nerve sheath tumors [6]. In particular, differentiation from schwannoma is essential, as schwannomas are usually encapsulated and display Antoni A and B areas, features absent in neurofibroma [7]. Similarly, atypical neurofibroma and low-grade malignant peripheral nerve sheath tumors must be excluded due to their clinical implications. When clinical findings are atypical, histopathological evaluation remains the decisive diagnostic tool [2].

Importantly, the present case highlights a clinically relevant diagnostic pitfall: the coexistence of an unusual pedunculated morphology and marked histopathological heterogeneity may complicate clinical and pathological interpretation despite representing a benign lesion. Recognizing this pattern is critical to avoid misinterpretation and ensure appropriate management. Solitary neurofibroma should be considered in atypical or heterogeneous cutaneous tumors, with diagnosis based on integrated clinicopathological evaluation.

Consent

The patient examination was conducted in accordance with the principles of the Declaration of Helsinki.

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